# Exhibit K

**DEPARTMENT OF HEALTH & HUMAN SERVICES**
Public Health Service
Food and Drug Administration
CENTER FOR DRUG EVALUATION AND RESEARCH

Division of Quality Surveillance Assessment
Inspection Assessment Branch
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January 17, 2017

Zhejiang Huahai Pharmaceutical Co. Ltd.
Xunqiao
Linhai, Zhejiang 317024
China

Reference FEI: 3003999190

Reference Inspection Date(s): November 14-18, 2016
Establishment Locale: Zhejiang Huahai Pharmaceutical Co. Ltd.
Xunqiao
Linhai, Zhejiang 317024
China

Dear Mr. Chen BaoHua:

We are enclosing a copy of the establishment inspection report (EIR) for the inspection that the U.S. Food and Drug Administration (FDA) conducted at your premises on the referenced locale and date(s). When the Agency concludes that an inspection is "closed" under 21 CFR 20.64(d)(3), it will release a copy of the EIR to the inspected establishment. This procedure is applicable to EIRs for inspections completed on or after April 1, 1997.

The Agency continually works to make its regulatory process and activities more transparent to the regulated industry. Releasing this EIR to you is part of this effort. The copy being provided to you comprises the narrative portion of the report; it may reflect redactions made by the Agency in accordance with the Freedom of Information Act (FOIA) and 21 CFR Part 20. This, however, does not preclude you from requesting additional information under FOIA.

If there is any question about the released information, feel free to contact me at: (301) 348-3088.

For more information on the U.S. FDA please visit our website at: www.fda.gov.

Sincerely,
Carla J. Lundi -S

Digitally signed by Carla J. Lundi -S
DN: c=US, o=U.S. Government, ou=HHS, ou=FDA, ou=People, cn=Carla J. Lundi -S, 0.9.2342.19200300.100.1.1=1300190859
Date: 2017.01.17 09:54:46 -08'00'

Carla J. Lundi, CSO
Inspection Assessment Branch

Enclosure: Establishment Inspection Report (EIR)

| **Establishment Inspection Report** | FEI: | **3003999190** |
|---|---|---|
| Zhejiang Huahai Pharmaceutical Co. Ltd. | EI Start: | 11/14/2016 |
| Linhai, Zhejiang, China | EI End: | 11/18/2016 |

TABLE OF CONTENTS



## SUMMARY


This routine current Good Manufacturing Practice (cGMP) and Pre-Approval (PAI) inspection of an Active Pharmaceutical Ingredient (API), Solid Oral Dosage, and Terminally Sterilized Finished Drug Product was conducted per FY17 work plans and assignment #46871. Pre-approval coverage was given to ANDA 209474 Levetiracetam for Injection. Coverage was given to compliance program 7346.832, Pre-Approval Inspections; compliance program 7356.002A, Sterile Drug Process Inspections; 7356.002, Drug Manufacturing Inspections; compliance program 7356.002F, Active Pharmaceutical Ingredient (API) Process Inspections; and compliance program 7356.021, Drug Quality Reporting System and NDA Field Alert Reports. The Quality, Facilities & Equipment, Production, Materials, and Laboratory systems received coverage.

The previous FDA inspection was conducted 7/12/2016-7/14/2016 for a preapproval inspection of oral solid dosage form products. The inspection was classified VAI. There was a 2-item FDA 483, Inspectional Observations, issued that included observations for: data was not documented contemporaneously and laboratory procedures for documentation were not followed in documentation of pre-analysis experiments. Corrective actions for the previously cited observations were evaluated during the current inspection and found that data was still not being documented contemporaneously. Additionally, the previous inspection found that the encapsulator required for the manufacturing of ANDA 207188 Paroxetine Capsules was not yet in place. Current inspection found there is now an encapsulator on site and under qualification.

The current inspection found the firm continues to manufacture API products and oral solid dosage drug products for the US market. At the conclusion of the inspection a 4-item FDA 483 was issued including observations for: procedures for controls of sterile products were not established and followed; laboratory methods and specifications were not scientifically sound; cleaning procedures were not established and followed; and data was not documented contemporaneously.

Firm management promised corrections to observations and committed to providing an initial written response within 15 business days. No samples were collected and there were no refusals. The facility has a current drug registration.

## ADMINISTRATIVE DATA

| | |
|---|---|
| Inspected firm: | Zhejiang Huahai Pharmaceutical Co. Ltd. |
| Location: | Xunqiao<br>Linhai, Zhejiang 317024, China |
| Phone: | +86-576-85016200 |
| Dates of inspection: | 11/14/2016, 11/15/2016, 11/16/2016, 11/17/2016, 11/18/2016 |
| Days in the facility: | 5 |
| Participants: | Justin A. Boyd, Investigator<br>Peter E. Baker, Investigator |

This was a joint inspection conducted by Investigator Boyd and Investigator Baker. Investigator Boyd served as the lead investigator. Portions of this report written by Investigator Boyd are identified with the initials "JAB". Portions of the report were written by Investigator Baker "PEB".

Translation was provided by a third party contractor Dr. Gu Zi Qiang, Pharmaceutical Consultant.

## HISTORY

(PEB)

The history of the firm has not changed significantly since the previous FDA cGMP inspection in 03/2015. An extensive history of the firm can be found in that FDA inspection report. A power-point presentation given at the opening meeting is attached as **Exhibit #12**. The firm continues to manufacture and export both APIs and Finished Dosage Forms to the United States. This was the initial inspection of the sterile manufacturing operations, and no sterile product is currently produced for any markets. This was the seventh FDA inspection of the "Xunqiao" facility.

Official FDA correspondence and FMD-145 correspondence to the most responsible individual onsite should be addressed to:

Mr. Chen BaoHua, General Manager
Zhejiang Huahai Pharmaceutical Co., Ltd.
Xunqiao
Linhai, Zhejiang 317024, China
Phone: +86 576 85016001
Email: chen@huahaipharm.com

The firm's US Agent for API is Xiaodi Guo, located at the following address:

Huaihai US Inc.
2002 Eastpark Blvd.
Cranbury, NJ 08512
Phone: 609-655-1688
Email: xguo@huahai pharmus.com

The firm's ANDA holder is Prinston Pharmaceutical Inc., which is a subsidiary of the Huahai group, and is located at the same address:

2002 Eastpark Blvd.
Cranbury, NJ 08512

**INTERSTATE COMMERCE**
(JAB)
This facility ships API and finished dosage products to the US market. A list of all finished dosage batches that have been shipped to the US market for 2015 and 2016 is included as **Exhibit #1.** A list of all API batches that were shipped to the US market is included as **Exhibit #13.** A list of all API batches that were transferred internally for manufacturing of finished dosage for the US market is included as **Exhibit #14.**

**JURISDICTION**
The firm manufactures Active Pharmaceutical Ingredients for the U.S. market. As such, the firm is subject to the adulteration provisions of section 501(a)(2)(b) of the Act, which requires all drugs to be manufactured in conformance with the current Good Manufacturing Practices outlined in 21 CFR 210/211. A list of all API products manufactured on site is included as **Exhibit #15.**

The firm also manufactures finished dosage drug products. A list of their finished dosage products is included as **Exhibit #2.**

**INDIVIDUAL RESPONSIBILITY AND PERSONS INTERVIEWED**
At the initiation of this inspection, we presented our FDA credentials and exchanged business cards with the most responsible person for this facility, Mr. Baohua Chen, General Manager. In addition

to Mr. Baohua Chen, a list of all personnel present for the initiation of the inspection is included as **Exhibit #3.**

This majority of inspectional information was provided by the following individuals:

- Jian Jing, Finished Drug Product QC Manager
- Zhu Yan, API QC Manager
- Jenson Ye, Vice President QA

The organizational charts are included as **Exhibit #4.**

Translation was provided by a third party contractor Dr. Gu Zi Qiang, Pharmaceutical Consultant.

**FIRM'S TRAINING PROGRAM**
(PEB)
I requested and reviewed the training history records for Ms. Zhu Zi Jun, an in-process control operator within the FDF manufacturing unit. We also requested and reviewed the training history file for a visual inspection operator for sterile liquid products. We found that the defect set used to challenge visual inspection operators was not maintained (**Observation #1.4**).

**MANUFACTURING/DESIGN OPERATIONS**
(JAB)
**Levetiracetam for Injection ANDA 209474**
The pre-approval portion of this inspection focused on the accuracy and completeness of data submitted in support of this ANDA, as well as the procedures, personnel, and equipment related to the proposed manufacturing processes. The firm currently manufactures no sterile products for any markets; therefore the firm performed a representative WFI fill on 17 November 2016 for our observation. The firm has historically manufactured a total of four Levetiracetam batches using the proposed manufacturing line located in building F1 Workshop #6; including one commercial size scale-up batch and three registration batches in support of ANDA 209474. This product will be terminally sterilized, profile SVT. This is the first drug application for a sterile injectable product from this site.

Workshop #6 is the only manufacturing line for injectable products on this campus. Filling operations had not been conducted since a development batch in June of 2016. Workshop #6 uses a Bosch filling machine inside of a RABS (Restricted Access Barrier System) with glove ports installed to perform set up and interventions. There is no procedure for preventatively changing the gloves, see **Observation #1**, and the acceptance criteria for the integrity testing of the glove was not justified, see **Observation #2.**